REMARKS

Claims 1-30 were pending in the above-identified application prior to entry of this Amendment. In this Amendment, claims 1, 2, 3, 4, and 7 have been amended and claims 14-30 have been withdrawn as being related to non-elected subject matter. Accordingly, after entry of this Amendment, claims 1-13 are pending in this case. The changes to the claims do not constitute the addition of new matter and full support for the changes may be found in the specification and claims as originally filed.

Rejection Under 35 U.S.C. §102(b)

Claims 1 and 2 have been rejected under 35 USC § 102(b) as allegedly be anticipated by Muller et al. (U.S. 4,329,347). This rejection is respectfully traversed.

The Examiner has stated "Muller et al teaches several structurally analogous compounds for use as cardiotonics and antithrombotics. See formula I on column 1 and note the definition of various variable groups. See column 2, method a wherein Muller discloses compound of formula II, which is also claimed in the instant claims. Example 1, on column 7 for the said compound." The compounds disclosed in the 347' patent, and most specifically recited by the Examiner, include carbostyril derivatives that include a substituent on the phenyl ring which is bonded to that ring through an ether linkage. In column 1 at formula 1 this substituent is defined as $-O\text{-}D\text{-}SO_m\text{-}R_2$. Thus, it can be seen from the definition of formual 1 that this substituent must not only include any ether linkage to the phenyl ring but a sulfur atom, either in the form of a sulfide, sulfoxide, or sulfonyl moiety.

In contrast to the carbostyril compounds disclosed in Muller, the compounds of the present invention do not include a substituent connected to the phenyl ring via an ether linkage which also includes a sulfur atom either in the form of a sulfide, a sulfoxide, or a sulfonyl moiety. For example, the substituent L as defined in the present application does not include moieties that would be bond to the phenyl ring via an ether linkage and also include sulfur atom in the form of a sulfide, sulfoxide, or a sulfonyl moiety.

With respect to compounds of formula II of the Muller patent, compounds of formula II are hydroxy substituted compounds wherein R_1 of Muller is hydrogen or alkyl of 1 to 3 carbon

atoms. Claims 1 and 2 as amended do not fall within the scope of formula II as described by Mueller. Specifically, the N-substituent as defined by Muller must be hydrogen or alkyl of 1 to 3 carbon atoms. The compounds of the present application would require such an N-substituent to be other than hydrogen or alkyl of 1 to 3 carbon atoms.

Claims 1 and 2 have also been rejected under 35 USC § 102(b) as allegedly be anticipated by Nishi et al. (U.S. 4,298,739). In support of his contention the Examiner has cited the carbostyril compounds of formula I on column 1 as well as the parent carbosytril compounds taught in the reference and those compounds cited at columns 3-6 and in Examples 1 to 473 at columns 26 through column 100. We respectfully traverse this rejection.

The compounds for formula I as disclosed in Nishi include a substituent on the phenyl ring which is bonded to that ring through an ether linkage. Furthermore, these substituents bound to the phenyl ring via an ether linkage must include an amide moiety. The claims as amended, currently do not include a substituent on the phenyl ring which would be bound to it via an ether linkage and also include an amide moiety. With respect to the parent carbostyril compounds taught in Nishi, the amended pending claims do not encompass such compounds as G is selected from alkyl, alkyl interrupted by one or more heteroatoms, cycloalkyl, cycloalkyl interrupted by one or more heteroatoms; and J is heterocycle optionally substituted with R_1 and R_2.

The Examiner has also rejected claims 1 and 2 under 35 USC § 102(b) as allegedly anticipated by Nakagawa et al. (U.S. 4, 298, 739). The Nakagawa reference listed on PTO form 892 however is US patent number 4,313,947. Given the description of the cited reference by the Examiner in paper No. 7 and the fact that U.S. Patent No. 4,313,947 is listed on the 892 form, the comments presented herein will be made with respect to the '947 patent. The rejection of claims 1 and 2 under 35 USC § 102(b) as being allegedly anticipated by Nakagawa 4,313, 947 is respectfully traversed.

Nakagawa discloses benzcycloamide derivatives which include a substituent on the phenyl ring which is bonded to that ring through an ether linkage. This substituent, in addition to

the ether linkage, includes at least 1 -CH=CH-, $-CH_2-$, $-CH(C_1-C_4$ alkyl)-, or $-C(C_1-C_4alkyl)_2-$ unit and an acid or ester moiety. The amended pending claims are compounds which do not include such a substituent bound to the phenyl ring of the disclosed compounds via an ether linkage and do not include Oalkylester or Oalkylacid substituents of the phenyl ring. With respect to the parent carbostyril compounds taught in Nakagawa, the amended pending claims do not encompass such compounds as G is selected from alkyl, alkyl interrupted by one or more heteroatoms, cycloalkyl, cycloalkyl interrupted by one or more heteroatoms; and J is heterocycle optionally substituted with R_1 and R_2.

The Examiner has also rejected claims 1 and 2 under 35 USC § 102(b) as allegedly anticipated by Nishi et al. (U.S. 4,435,404). This rejection is respectfully traversed.

The compounds disclosed in the 404' patent, and represented by formula I recited therein, are carbostyril derivatives which include a substituent on the phenyl ring which is bonded to that ring through an ether linkage. This substituent bound via an ether linkage also includes an amide moiety. The amended pending claims do not include compounds which include such an amide containing substituent bound to the phenyl group via an ether linkage. With respect to the parent carbostyril compounds taught in Nishi, the amended pending claims do not encompass such compounds as G is selected from alkyl, alkyl interrupted by one or more heteroatoms, cycloalkyl, cycloalkyl interrupted by one or more heteroatoms; and J is heterocycle optionally substituted with R_1 and R_2.

Claims 1 and 2 have been rejected under 35 USC § 102(b) by being anticipated by Richter Beilstein Handbuch der Organischen Chemie 4, Aufl. 1 EW 20-22, 1935. This rejection is respectfully traversed.

The claims have been amended such that G is selected from alkyl, alkyl interrupted by one or more heteroatoms, cycloalkyl, cycloalkyl interrupted by one or more heteroatoms; and J is heterocycle optionally substituted with R_1 and R_2. Thus, the compounds disclosed by Richter do not fall within the scope of the amended pending claims 1 and 2.

Given the amendments to the claims, and the arguments set forth above, it is submitted that the references cited by the Examiner as a basis for rejections under 35 USC 102(b) do not teach each and every element of the invention as defined by the amended pending claims and therefore are not anticipatory.

In view of these amendments and remarks, withdrawal of the rejections under 35 U.S.C. §102(b) is respectfully requested.

Rejection Under 35 U.S.C. §103(a)

The examiner has rejected claims 1 and 2 under 35 U.S.C. §103 as allegedly obvious in light of Nishi et al. (U.S. 4,298,739) and Nishi et al. (U.S. 4,435,404). These rejections are respectfully traversed. The examiner has also rejected claims 1 and 2 under 35 U.S.C. §103(a) as allegedly obvious in light of Nakagawa et al. (U.S. 4,298,739). The Nakagawa reference listed on PTO form 892 however is US patent number 4,313,947. Given the description of the cited reference by the Examiner in paper No. 7 and the fact that U.S. Patent No. 4,313,947 is listed on the 892 form, the comments presented herein will be made with respect to the '947 patent. The rejection of claims 1 and 2 under 35 USC § 103(a) as being allegedly obvious in light of Nakagawa 4,313, 947 is respectfully traversed.

As the examiner has stated with respect to the '739 and '404 patents:

> "[I]nstant claims differ in requiring variously substituted quinolone compounds including the aryl ring, side chain L and the nitrogen of quinolone.
> As seen, Nishi et al. permits various substituents in the carbostyril but exemplifies not all of them."

The same statement was made with respect to Nakagawa et al.

As set forth in M.P.E.P. § 2143, "[t]o establish a *prima facie* case of obviousness, three basic criteria must be met. *First*, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art,

to modify the references or to combine reference teachings. *Second*, there must be a reasonable expectation of success. *Finally*, the prior art references (or references when combined) must teach or suggest all of the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must be found in the prior art, not in the Applicants' disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991)." As the Federal Circuit has also stated, "[a] general incentive does not make obvious a particular result, nor does the existence of techniques by which those efforts can be carried out." *In re Deuel*, 34 USPQ2d 1210, 1216 (Fed. Cir. 1995).

As the examiner has suggested, Nishi and Nakagawa do exemplify a variety of substituted quinolone compounds including an aryl ring, side chain and quinolone nitrogen. They do not however teach or suggest that one make the compounds as presently disclosed. One reading Nishi's and Nakagawa's disclosed list of carbostyril derivatives would not necessarily be lead to produce the compounds presently claimed. Additionally, there is no reasonable expectation that the claimed compounds could be produced or would succeed as serine protease inhibitors in view of Nishi and Nakagawa.

Additionally, Nishi and Nakagawa, alone or in combination, do not teach or suggest all of the claim limitations. The compounds as presently claimed, including the definitions of the N-substituents and the phenyl ring substituents, are simply not disclosed in either Nishi or Nakagawa.

At best, the carbostyril compounds disclosed by Nishi and Nakagawa might serve as a basis for which one might *try* to produce carbostyril derivatives possessing serine protease inhibitory activity. What is obvious to try however is not the standard for obviousness under 35 U.S.C. § 103(a) (See, *In re O'Farrell*, 853 F.2d 894, 7 USPQ2d 1673 (Fed. Cir. 1988). Nishi and Nakagawa give no indication as to which substituents are critical and no direction as to which of many possible choices is likely to be successful. Nishi and Nakagawa simply serve as a basis for which one might try to vary all the parameters with respect to each of numerous possible substituents until one possibly arrived as a successful result.

In view of these amendments and remarks, withdrawal of the rejections under 35 U.S.C. §103(a) are respectfully requested.

Rejection Under 35 U.S.C. §112, Second Paragraph

The examiner has rejected claims 1-10 under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter of the invention. This rejection is respectfully traversed.

Claims 1, 2, 3, and 4 have been amended and no longer include the term "prodrug." Thus, it is respectfully submitted that the rejection of claims 1-10 under 35 U.S.C. §112, second paragraph has been addressed and rendered moot.

In view of these amendments and remarks, withdrawal of the rejections under 35 U.S.C. §112, second paragraph, is respectfully requested.

The above discussion and corresponding Amendments are based on section 112 issues and are not made to overcome art-based rejections. Accordingly, such discussion and corresponding Amendments should not be construed in a limiting manner.

It is respectfully submitted that the claims have been put in condition for allowance. Notification to this affect is earnestly solicited. The Examiner is encouraged to contact the Applicants' undersigned attorney to discuss this matter if any questions should arise upon further examination of the pending claims.

Respectfully submitted,

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Date

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